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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,575	09/30/2003	Sudhir K. Sinha	P56885	2640

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EXAMINER	
BABIC, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/673,575	SINHA ET AL.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1, 5-9, 21, and 22 are pending. The following Office Action is in response to Applicant's response dated August 16, 2006.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Upon further consideration, the following new ground(s) of rejection is made in view of previously considered prior art.

1. Claims 1, 7, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Keller et al. ("Molecular evolution of the CMT1A-REP region: a human- and chimpanzee-specific repeat. Mol Biol Evol. 1999 Aug;16(8):1019-26").

With regard to claim 1, it is initially noted that the phrase --for quantitating a human DNA in a sample-- is considered an *intended use* of the method and does not incorporate a patentably distinct feature.

Keller et al. teach a method (pages 1020, 1021, materials and methods, for example) comprising: providing a sample to be analyzed (page 1020, materials and methods, non-human primate samples, for example); amplifying predetermined genomic DNA containing an Alu element by using primers (figure 1, primers P1/C1, P2/T1, D1/C1, T1/D2; pages 1020, 1021, materials and methods, polymerase chain reaction, for example), said Alu element being enriched in the human genome (page 1023, figure 3c, lane hu, for example) compared to non-human primates genomes (page 1023, figure 3c, lanes go-ga, for example); the amplification being intra-Alu polymerase chain reaction amplification (figure 1, primers P1/C1, P2/T1, D1/C1, T1/D2; pages 1020, 1021, materials and methods, polymerase chain reaction, for example); and *measuring the amount* the human DNA by comparing the amplified DNA with a reference (page 1023, figure 3c). Keller teaches DNA analysis using ethidium stained gels (page 1023, for example). Ethidium stained gels show, based on fluorescence, that one lane has a greater or lesser *quantity* of DNA than another. The claims does not require that specific units of measurement determined with processes such as quantitative PCR. Thus, in a broader sense, agarose gel electrophoresis is a quantitative procedure that *measures the amount* of DNA .

With regard claim 7, Keller teaches detecting the human DNA on an agarose gel stained with ethidium bromide (Page 38, Column 2, Paragraph 1).

With regard to claim 21, the teachings of Keller as they anticipate claim 1 also anticipate claim 21. Keller teaches a method wherein the Alu element is present *only* within the human genome (i.e. comparison between lane hu and lanes go-ga, for

example). It is noted that Keller also teaches methods wherein the Alu is present in both human and non-human genomes (i.e. comparison between lanes hu and lanes pc-cc, for example), however, the teachings of Keller still anticipate the claimed invention because it is claimed in "comprising" language, which allows for the incorporation of additional method steps.

Response to Arguments - Claim Rejections - 35 USC § 102

Applicant's arguments with respect to the previously applied references have been fully considered but they are not persuasive.

Rejection of claim(s) 1, 7, and 21 over Keller

Applicant asserts that Keller fails to show, "said Alu element being enriched in the human genome compared to non-human primate genomes," within a reasonable interpretation of the claim language. This is not persuasive because absent of any specific definition of the term, "enriched" within the specification, it is asserted that the teachings of Keller, namely the comparison of amplification observed in human species as opposed to non-human primate species anticipate the claimed language. The term, "enriched" can be interpreted to mean an Alu sequence appearing in the human genome and not in another non-human primate genome.

Applicant further submits that Keller does not show, "copy number" of the Alu sequences. This is not persuasive because it is not commensurate in scope with the

claimed invention. The claimed invention does not require the detection of determination of, "copy number" of the Alu sequence.

Applicant further asserts that Keller fails to show, " measuring the amount of the human DNA by comparing the amplified DNA with a reference--," within a reasonable interpretation of the claim language. The Examiner continues to maintain that the above limitation is broad in nature with respect to applicable prior art and is being interpreted as such. Claim 1 recites *measurement by comparison* with a reference, which is clearly encompassed by the visual comparison one can make with an ethidium stained gel.

Applicant appears to further submits that Keller does not show, "copy number" of the Alu sequences. This is not persuasive because it is not commensurate in scope with the claimed invention. The claimed invention does not require the detection of determination of, "copy number" of the Alu sequence.

Claim Rejections - 35 USC § 103

The rejections of claim(s) 1 and 7 over Palmirotta in view of Brooks-Wilson of have been withdrawn in view of Applicant's arguments. Upon further review, Brooks-Wilson does not teach intra-Alu PCR. Thus, all subsequent rejections reliant upon Palmirotta in view of Brooks-Wilson are withdrawn as well.

The rejections of claim(s) 1, 7, 21, and 22 over Carroll in view of Brooks-Wilson of have been withdrawn in view of Applicant's arguments. Upon further review, Brooks-

Wilson does not teach intra-Alu PCR. Thus, all subsequent rejections reliant upon Carroll in view of Brooks-Wilson are withdrawn as well.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Upon further consideration, the following new ground(s) of rejection is made in view of previously considered prior art.

1. Claims 1, 7, 8, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of

genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434).

With regard to claim 1 and 22, Sifis et al. teach a method (pg. 589, 590, materials and methods, for example) comprising: providing a sample to be analyzed (pg. 589, 590, materials and methods, amplification, for example); amplifying predetermined genomic DNA containing an Alu element by using primers (pg. 589, 590, materials and methods, amplification, for example), the amplification being intra-Alu polymerase chain reaction amplification (pg. 589, 590, materials and methods, amplification, for example); and *measuring the amount* the human DNA by comparing the amplified DNA with a reference (fig. 1, 2; pg. 589, 590, materials and methods, amplification, for example). Sifis further teaches that the assay is based on the amplification of core Alu sequences from primate DNA (pg. 590, col. , however, does not expressly teach the Alu sequences as being enriched in the human genome as compared with non-human primates.

Palmirotta provides a supporting disclosure that teaches the PCR of Alu sequences for the specific purpose of determining the origin of the DNA (i.e. human DNA or non-human primate DNA) (pg. 432, col. 1, for example). The teachings of Palmirotta clearly demonstrate that selection of an Alu sequence that occurs in humans as well as non-human primates can lead to inconclusive results.

It is further submitted that it was routine practice to one of skill in the art at the time of invention to incorporate controls within experiments to test for correct function of the procedure or process.

Thus, a practitioner of ordinary skill in the art at the time of invention wanting to quantify human DNA from an unknown source through the method of Sifis would have been motivated select an Alu known to reside strictly within the human genome to obtain accurate human results. The practitioner would have been further motivated to test non-human primate controls with the unknown sample to confirm correct results.

With regard to claim 7, Palmirotta teaches detecting the human DNA on an agarose gel stained with ethidium bromide (Figure 1).

With regard to claim 8, Sifis teaches detecting the human DNA using a quantitative PCR system (pg. 590, col. 1, for example).

2. Claims 5 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252), Buck et al. ("Design Strategies and Performance of Custom DNA Sequencing Primers") BioTechniques. September 1999. 27: Pages 528-536).

Regarding Claim 5, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not expressly disclose the *exact* primer sequences of SEQ ID NO: 3 and SEQ ID NO: 4, drawn to the "young" Yb8 Alu subfamily.

Jurka discloses the entire Sb2 Alu subfamily sequence (Figure 1). The term "Sb2" is considered to older nomenclature of the "young" Yb8 subfamily (See reference: Batzer et al. "Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, Pages 3-6).

The *identical* sequence presented in SEQ ID NO: 3 (5'-CGAGGCGGGTGGATCATGAGGT-3' is contained in the sequence provided by Jurka (Figure 1) from nucleotides 48-69. Furthermore, the *identical* complement of the sequence (i.e. reverse primer) presented in SEQ ID NO: 4 (5'-TCTGTCGCCCAGGCCGGACT -3' is contained in the sequence provided by Jurka (Figure 1) from nucleotides 273-254.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have

> similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties"

Since the claimed primers simply represent complementary functional homologs of the sequences taught by Jurka, the claimed primers are *prima facie* obvious over Jurka in view Buck et al.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

3. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Regarding claim 9, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

Gelmini et al. disclose the practice of a quantitative PCR system using *Taq*Man chemistry (Figures 1,2,3; Table 1; Page 754, Columns 1,2). Furthermore, they highlight the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (Page 752, Column 2, Paragraph 2).

It would have been *prima facie* obvious to a practitioner ordinary skill in the art at the time of invention to incorporate a quantitative PCR system into the methods of Sifis since Gelmini suggests such a modification for among other reasons, to circumvent post-PCR product quantitation procedures.

4. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Keller et al. ("Molecular evolution of the CMT1A-REP region: a human- and chimpanzee-specific repeat. Mol Biol Evol. 1999 Aug;16(8):1019-26") in view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Regarding claim 9, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

Gelmini et al. disclose the practice of a quantitative PCR system using *Taq*Man chemistry (Figures 1,2,3; Table 1; Page 754, Columns 1,2). Furthermore, they highlight the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (Page 752, Column 2, Paragraph 2).

It would have been *prima facie* obvious to a practitioner ordinary skill in the art at the time of invention to incorporate a quantitative PCR system into the methods of Keller since Gelmini suggests such a modification for among other reasons, to circumvent post-PCR product quantitation procedures.

Response to Arguments - Claim Rejections - 35 USC § 103

Applicant's arguments with respect to the previously applied references have been fully considered but they are not persuasive.

Rejection of claim(s) 5 and 21 over Sifis in view of Palmirotta, Jurka, and Buck

Applicant asserts there is no desirability of using the claimed sequences on the basis of the prior art references, making specific references to *In re Deuel.*

The Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, **however**, the Court stated,

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships **may provide the requisite motivation or suggestion** to modify known compounds to obtain new compounds. For example, a prior art compound **may suggest** its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties"

Since the claimed primers simply represent complementary functional homologs of the sequences taught by Jurka, the claimed primers are *prima facie* obvious over Jurka in view Buck et al. The teachings of Buck clearly show that every primer of *a known sequence* would have a reasonable expectation of success.

Furthermore, a practitioner of ordinary skill in the art at the time of invention wanting to quantify human DNA from an unknown source through the method of Sifis would have been motivated select an Alu known to reside strictly within the human genome to obtain accurate human results.

Rejection of claim(s) 9 over Keller or Sifis view of Palmirotta and Gelmini

Applicant asserts there is no reason to perform measurement of the amount of the human DNA within the cited methods. As noted in MPEP 2144, "The strongest rationale for combining references is a recognition that some advantage or expected beneficial result would have been produced by their combination." The advantages of the methods of Gelmini are clearly outlined within the rejection.

Allowable Subject Matter

As noted previously, claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

None of the previously applied references teach or suggest the amplification of the AluYd6 subfamily of human specific Alu elements. The sequences presented in SEQ ID NOs: 5 and 6 are novel and unobvious over the prior art.

Conclusion

Claims 1, 5, 7-9, 21, and 22 are rejected.

Claim 6 is objected to.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-

272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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